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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/538,793 | 06/10/2005 | Jun Tomono | TOMON03 | 8821 |

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| EXAMINER | |
|---|---|
| MAKAR, KIMBERLY A | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/538,793 | TOMONO ET AL. | |
| | Examiner | Art Unit | |
| | Kimberly A. Makar | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4 and 6-10* is/are rejected.

7)☒ Claim(s) *3 and 5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/04/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Double Patenting*

### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 2, and 6-10 are rejected under 35 U.S.C. 102(b) as being taught by Yamanaka et al (Mutation Analysis of the 5' Untranslated Region of the Cold Shock CspA mRNA of Escherichia coli. Journal of Bacteriology, 1999. 6284-62910) listed in applicant's 1449 IDS form dated 08/04/2005. Claims 1, 2, and 6-10 recite a vector having a portion encoding a 5'UTR derived from an mRNA for a cold shock protein gene, wherein a mutation is introduced into the 5'UTR such that a distance between stem structures is formed in that region (claim 1). The vector is further limited wherein the mutation is an insertion or a deletion (claim 2) and wherein the vector has a promoter located upstream of the 5'UTR (claim 6). The vector is further limited wherein

the vector comprises a sequence that is complementary to an anti-downstream box sequence in a ribosomal RNA of a host to be used, wherein said nucleotide sequence is located downstream of the portion encoding a 5'UTR (claim 7) and wherein the vector is a plasmid (claim 8). Claim 9 recites a method for expressing a protein of interest, comprising 1) transforming a host cell with the vector defined in claim 1 into which a gene encoding a protein of interest have been incorporated to obtain a transformant; 2) culturing the transformant; and 3) shifting the culture temperature down to one lower than a conventional temperature to express the protein. The method is further limited wherein a promoter is induced during or after the reduction of temperature (claim 10).

3. Yamanaka teaches a series of plasmid vectors comprising mutations of the cold shock protein CspA 5'UTR and gene operably linked to a lacZ reporter gene (see abstract). The plasmids are generated by deletion of specific portions of the CspA 5'UTR (see figure 1) which cause changes in the region where the deletions are located which results in changes in the stem loop structures in the regions where the deletions occur (see figure 6). These vectors are driven by the CspA promoter which is located upstream of the CspA 5'UTR (see figure 1, cross-hatched bars). Additionally, Yamanaka teaches that the CspA mRNA contains a 14-base downstream box, located 12 base pairs from the initiation codon (i.e. downstream of the 5'UTR) which is complementary to a 16S rRNA of e. coli, which is called anti-downstream box (page 6284). Yamanaka teaches vectors pMM67, pMM023, pMM024, pMM025 and pMM026 (figure 1A) as well as pMM07, pKNJ37, pKM67 and pKNJ38 (figure 5A) which all have the wild-type anti-downstream box maintained. Thus Yamanaka teaches the anti-

downstream box sequence to a ribosomal RNA of the host used wherein the anti-downstream box is located downstream of the 5'UTR.

4. Additionally Yamanaka teaches a method of producing lacZ (protein of interest) by transforming cells with the vectors pMM07, pKNJ37, pKM67 and pKNJ38 into e. coli AR137 and culturing the cells at 37°C and then reducing the temperature to 15°C (see Material and Methods, beta-galactosidase assay section, page 6285). Yamanaka teaches that plasmids pKM67 and pKNJ38 which has low beta-galactosidase expression at 37°C (time 0) both had significant increases in beta-gal activity at 15°C (see5B and text on page 6288). Thus Yamanaka teaches a method of producing a protein by the induction of a promoter with a reduction in temperature.

5. Thus Yamanaka teaches the claimed invention.

6. Claims 1, 2, 4, and 6-10 are rejected under 35 U.S.C. 102(e) as being taught by Inouye et al (US Patent No. 6,610,533). Claims 1, 2, 4, and 6-10 recite a vector having a portion encoding a 5'UTR derived from an mRNA for a cold shock protein gene, wherein a mutation is introduced into the 5'UTR such that a distance between stem structures is form in that region (claim 1) The vector is further limited wherein the mutation is an insertion or a deletion (claim 2) wherein the portion encoding a 5' UTR further has an operator (claim 4) or wherein the vector has a promoter located upstream of the 5'UTR (claim 6). The vector is further limited wherein the vector comprises a sequence that is complementary to an anti-downstream box sequence in a ribosomal RNA of a host to be used, wherein said nucleotide sequence is located downstream of

the portion encoding a 5'UTR (claim 7) and wherein the vector is a plasmid (claim 8). Claim 9 recites a method for expressing a protein of interest, comprising 1) transforming a host cell with the vector defined in claim 1 into which a gene encoding a protein of interest have been incorporated to obtain a transformant; 2) culturing the transformant; and 3) shifting the culture temperature down to one lower than a conventional temperature to express the protein. The method is further limited wherein a promoter is induced during or after the reduction of temperature (claim 10).

7. Inouye et al (US Patent No. 6,610,533) teaches a series of plasmid vectors comprising mutations of the cold shock protein CspA 5'UTR and gene operably linked to a lacZ reporter gene (see abstract). The plasmids are generated by deletion of specific portions of the CspA 5'UTR (see figures 9A and 13A) which cause changes in the region where the deletions are located which results in changes in the stem loop structures in the regions where the deletions occur (see figure 14A-F). These vectors are driven by the CspA promoter which is located upstream of the CspA 5'UTR (see figure 9A, cross-hatched bars). Additionally, Inouye teaches that the CspA mRNA contains a 14-base downstream box, located 12 base pairs from the initiation codon (i.e. downstream of the 5'UTR) which is complementary to a 16S rRNA of e. coli, which is called anti-downstream box (column 2, lines 51-66). Inouye teaches vectors pMM67, pMM023, pMM024, pMM025 and pMM026 (figure 9A) as well as pMM07, pKNJ37, pKM67 and pKNJ38 (figure 13A) which all have the wild-type anti-downstream box maintained. Thus Inouye teaches the anti-downstream box sequence to a ribosomal

RNA of the host used wherein the anti-downstream box is located downstream of the 5'UTR.

8. Furthermore, Inouye teaches the incorporation of the lac operator, into a truncated 5'UTR of CspA regulatory regions (Example 12, column 35, lines 40-45) to form plasmid vectors pINZ and pINZDB1 (see figure 17A). These vectors maintain 17 base pairs of the 5'UTR of CspA. Thus Inouye teaches a vector encoding a 5'UTR derived from a cold shock protein gene, wherein a deletion is introduced into the 5'UTR and the vector further comprises an operator in the 5'UTR.

9. Additionally Inouye teaches a method of producing lacZ (protein of interest) by transforming cells with the vectors pMM07, pKNJ37, pKM67 and pKNJ38 into e. coli AR137 and culturing the cells at 37°C and then reducing the temperature to 15°C (examples 1, 2, 3, 5, 6, 7, etc). Inouye teaches that plasmids pKM67 and pKNJ38 that have low beta-galactosidase expression at 37°C (time 0) both had significant increases in beta-galactivity activity at 15°C (see figure 13B). Thus Inouye teaches a method of producing a protein by the induction of a promoter with a reduction in temperature.

10. Thus Inouye teaches the claimed invention.

***Conclusion***

11. Claims 3 and 5 are free of the art. Claims 3 and 5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KAM/09/29/06

DAVID GUZO
PRIMARY EXAMINER